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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/560,497	12/12/2005	Lars Terje Holmaas	PN0324	4578

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GE HEALTHCARE, INC.
IP DEPARTMENT
101 CARNEGIE CENTER
PRINCETON, NJ 08540-6231

EXAMINER

KATAKAM, SUDHAKAR

ART UNIT	PAPER NUMBER
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1621

MAIL DATE	DELIVERY MODE
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10/29/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/560,497

Applicant(s)

HOLMAAS ET AL.

Examiner

Sudhakar Katakam

Art Unit

1621

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 September 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-21 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-21 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- ☐ Notice of Informal Patent Application
- ☐ Other: _____

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/25/07 has been entered.

Response to Arguments

2. Applicants' arguments filed on 25th September 2007 have been fully considered but they are not persuasive.

Applicants' argued that no prior art document suggests using 1-methoxy-2-propanol as a solvent in the alkylation step. Knowing that 1-methoxy-2-propanol is used as the solvent in the purification by recrystallization of iohexol, one skilled in the art would not expect that a solvent mixture that is dominated by the same solvent would also be used in the alkylating step. The reason for this is that in the alkylation step it is required that the solvent shows good solubility for 5-(acetamido)-N,N'bis(2,3-dihydroxypropyl)-2,4,6-triiodoisophthalamide and that the product (iohexol) does not precipitate during the reaction, whereas in the purification step the solvent used should show little solubility for the product.

The examiner does not find these arguments persuasive. **Malthe-Sorensen** clearly suggests to one having ordinary skill in the art the use of similar solvents. After all it is routine for skilled artisan to use art recognized alternative solvents. So, it would

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have been obvious to a person of ordinary skill in the art at the time of the invention was made, to use 1-methoxy-2-propanol in **Malthe-Sorensen** with a reasonable expectation of success.

Applicants allege that even though the solvents in question only differ by one carbon, they act very differently by using 1-methoxy-2-propanol as a reaction solvent in their process, but have not shown this in a side-by-side comparison with the closest prior art.

So, it would have been obvious to a person of ordinary skill in the art at the time of the invention was made, to use 1-methoxy-2-propanol in **Malthe-Sorensen**, with a reasonable expectation of success of making the final product in the prior art.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1, 3-4, 7-9, 11-12, 14-15, 17, and 19-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Malthe-Sorensen (US 5,948,940).

Instant claims are drawn to a process for the preparation of iohexol comprising alkylating 5-(acetamido)-N,N'-bis(2,3-dihydroxypropyl)-2,4,6-triiodoisophthalamide with a 2,3-dihydroxypropylating agent, such as 1-chloro-2,3-propandiol, in the presence of a base and of a solvent comprises a C₁-C₅-monoalkylether of a C₃-C₁₀ alkylene-glycol. The process further comprise a one or more co-solvents comprises C₁-C₄ alkanols

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and/or water. The solvent used in an amount of 0.5 to 5 ml per gram 5-acetamide. The claims further contain the purification of crude iohexol obtained from the above process using solvent and co-solvent. The purification is performed by crystallizing and separation of the iohexol from the said solvent. Crystalline isohexol is washed with isopropanol.

Malthe-Sorensen et al disclose a process for the production of iohexol, said process comprising reacting 5-(acetamido)-N,N'-bis(2,3-dihydroxypropyl)-2,4,6-triiodoisophtalamide with a 2,3-dihydroxypropylating agent in the presence of a base and a solvent, viz., **2-methoxy-ethanol** (col 2, lines 1-7) which is a C₁-C₅-monoalkylether of a C₃-C₁₀ alkylene-glycol. The example discloses that the solvent, viz., 2-methoxy-ethanol (278 ml) per 283g of 5-acetamide (see example 1). It also discloses the purification of crude iohexol using **2-methoxy-ethanol**, which is a C₁-C₅-monoalkylether of a C₃-C₁₀ alkylene-glycol, as solvent and isopropanol, which is a C₁-C₄ alkanol, as a co-solvent. The crude iohexol purified preferably by recrystallization using the isopropanol (see col.3, lines 8-40).

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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6. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

7. Claims 1-2, 5-6, 10, 13, 16, 18 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Malthe-Sorensen et al** (US 5,948,940).

Instant claims are further limited to solvent, viz., 1-methoxy-2-propanol, and its concentration in the process.

Malthe-Sorensen et al teaches a process for the production of iohexol, said process comprising reacting 5-(acetamido)-N,N'-bis(2,3-dihydroxypropyl)-2,4,6-triiodoisophthalamide with a 2,3-dihydroxypropylating agent in the presence of a solvent, viz., **2-methoxy-ethanol** (col 2, lines 1-7). It also teaches the purification of crude iohexol using **2-methoxy-ethanol** as solvent and isopropanol as a co-solvent.

The difference between the instant invention and **Malthe-Sorensen et al** is that the instant invention used the **1-methoxy-2-propanol**, whereas the reference used **2-methoxy-ethanol**.

It would have been obvious to a person of ordinary skill in the art, at the time of present invention was made, to have modified the reference's teachings by using an alternative solvent, such as **1-methoxy-2-propanol** with a reasonable expectation of success. Please note that the solvent differs by one carbon. One skilled in the art would

have been motivated to substitute one solvent for another based on such factors as cost and availability of said solvents.

Some limitations of the dependent claims may not be expressly disclosed in Malthe-Sorensen et al. However, these limitations, such as concentrations of the solvent, appear to be drawn to tweaking the process conditions. Changing such parameters is prima facie obvious because an ordinary artisan would be motivated to optimize a process. Merely modifying the process conditions such as temperature and concentration is not a patentable modification absent a showing of criticality. In re Aller, 220 F.2d 454, 105 U.S.P.Q. 233 (C.C.P.A. 1955).

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sudhakar Katakam whose telephone number is 571-272-9929. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 571-272-0871. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a

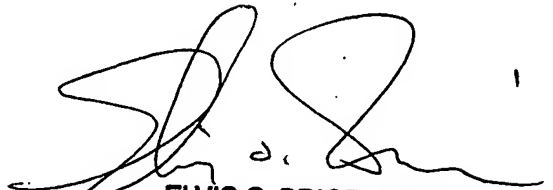
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USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SK



ELVIS Q. PRICE, PH.D.
PRIMARY EXAMINER